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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,502	02/16/2006	Yutaka Hanazono	1422- 0708PUS1	9981

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
10/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,502	HANAZONO ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2008 and 07 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed July 24, 2008 and August 7, 2008 have been fully considered but they are not persuasive. The declaration under 37 § CFR 1.132 by Dr. Yutaka Hanazono, filed August 7, 2008 has been considered but is not persuasive for the reasons set forth below.

The rejection of claim 5 under 35 U.S.C. § 102/103 made in the office action mailed March 24, 2008 has been withdrawn.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 6-9 rejected under 35 U.S.C. 103(a) as being unpatentable over Zanjani et al. (1996) Internatl. J. Hematol., vol. 63, pp. 179-192 in view of Li et al. (2001) Blood, Vol. 98, pp. 335-342 and Sone et al. (April 2003), Circulation, Vol. 107, pp. 2085-2088 and further in view of Hamaguchi et al. (1999) Blood, Vol. 93, pp. 1549-1556 for reasons set forth in the office action mailed March 24, 2008.

Zanjani teaches the engraftment of human hematopoietic cells in fetal sheep by administering the human cells to the sheep fetus in utero to expand the cells (page 181,

col. 2, parag. 1, lines 16-22). The engrafted sheep fetus is carried to term, whereby human IL-3, Stem Cell Factor, GM-CSF or c-Kit ligand were administered to the chimeric sheep, resulting in a significant increase human hematopoietic cells in the bone morrow of the sheep (page 184, col. 1, lines 3-11 and page 185, Table 4). The metaphase analysis discussed in Table 4 indicates separation of the human cells from the sheep. The increased human hematopoietic cell component in sheep bone marrow provides motivation to employ the method of Zanjani to expand human hematopoietic stem cells in the chimeric sheep model.

Li teaches the differentiation of primate ES cells into hematopoietic cells by culturing the ES cells on S17 bone marrow stromal cells in a media comprising BMP-4, whereby the number of expandable cultures increase 18 fold over cultures lacking BMP-4 (page 337, col. 2, parag. 2, line 3 to page 338, col. 1, line 6). Thus, motivation is clearly present for the differentiation of primate ES cells in the presence of BMP-4.

Sone teaches the differentiation of primate ES cells when cultured on OP9 bone marrow stromal cells (page 2086, col. 1, parag. 2, lines 1-4). Hamaguchi provides specific motivation for co-culture with OP9 stromal cells as they M-CSF and thus are preferable because they do not induce macrophage production which in turn damages stromal cells (page 1553, col. 1-2, bridg. parag.).

Therefore at the time of the instant invention, it would have been obvious to the ordinary artisan to modify the method of Zanjani by administering primate/monkey/human hematopoietic cells differentiated in vitro by the method of Li and Sone in view of Hamaguchi. The combination of art provides sufficient motivation to

combine the art to expand, as taught by Zanjani, the in vitro produced hematopoietic cells given the above cited motivation.

Applicant argues in the present invention an embryonic stem cell is transplanted to fetal sheep so are to prepare a human/sheep hematopoietic chimera. The argument is based on the declaration by Dr. Hanazono. Applicant has also supplied a reference, Kyba et al, to support their allegations. This argument is not persuasive.

The claims do not require implantation of a human embryonic stem cell into a fetal sheep to produce a human/sheep hematopoietic chimera. Indeed, the claims require maintaining a primate embryonic stem cell under conditions suitable for differentiation into a hematopoietic cell, and transplanting the resulting cells. When a primate ES cell is maintained under conditions suitable for differentiation into hematopoietic cell, the resulting cells are hematopoietic cells. Thus, the implanted cell is a hematopoietic stem cell, not an embryonic stem cell as claimed... The subject matter applicant states is in the claim, in fact is not.

The art cited by applicant has been reviewed, and while applicant may have accomplished something unexpected, the claims are not so written. Further, the Kyba teaches the in vitro differentiation of embryonic stem cells into EB's and implanting EB cells, cells which are not embryonic stem cells. (See Kyba, page 996, col. 1, parag. 2, lines 1-4). EB-derived cells are not embryonic stem cells, and Kyba further states the cells a or the hematopoietic lineage. Further, Kyba states the EBD's failed to generate CFU-S. It is further noticed the specification does not contemplate the implantation of embryonic stem cells, but hematopoietic cells (specification, page 31, (2). Thus,

applicant's arguments do not reflect the disclosure, the claims or the status of the art at the time of filing.

The cited prior art meets the limitations of the claims by teaching the induction of hematopoietic cells from embryonic stem cells in vitro and transplantation of such induced cells into fetal sheep.

Further, should applicant further arguments regarding unexpected results, applicant should remember, the scope of the claims has to correlate with the unexpected results.

Applicant's comments regarding KSR have been considered, however, they are not persuasive. The claims require the implantation of hematopoietic cells into a fetal sheep. The hematopoietic cells are derived from ES cells. The art clearly teaches the production of hematopoietic cells from ES cells in vitro. Additional art is supplied to teach the production of sheep hematopoietic chimeras. While applicant argues nonobviousness in view of failures of implanting ES cells, the arguments to not address implanting hematopoietic cells, or hematopoietic stem cells.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

October 22, 2008